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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/589,102	10/05/2007	Tae-Yoon Kim	SIGONG-13046	5838
72960	7590	12/28/2009		
Casimir Jones, S.C. 2275 DEMING WAY, SUITE 310 MIDDLETON, WI 53562			EXAMINER NOBLE, MARCIA STEPHENS	
			ART UNIT	PAPER NUMBER
			1632	
			MAIL DATE	DELIVERY MODE
			12/28/2009	PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

# Office Action Summary

## Application No.

10/589,102

## Applicant(s)

KIM ET AL.

## Examiner

MARCIA S. NOBLE

## Art Unit

1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 05 November 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1-17 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 1-10 is/are allowed.
- 6) ☒ Claim(s) 11-15 is/are rejected.
- 7) ☒ Claim(s) 16 and 17 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 10 August 2006 is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

## Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

## Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB06)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

## **DETAILED ACTION**

### ***Continued Examination Under 37 CFR 1.114***

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11/5/2009 has been entered.

### ***Withdrawn Rejections***

The rejection of claims 16 and 17, under 35 U.S.C. 102(e) as being anticipated by Cao et al (US2003/0233675 pub date 12/18/2003; filing date 2/20/2003 now Patent Number 7,314,974), is withdrawn.

Applicant amendment the claims to recite that the oligonucleotide "consists of" the sequence of SEQ ID NO:1. Cao discloses a sequence comprising SEQ ID NO:1 and additional sequences. Therefore, Cao no longer anticipates the claims.

The rejection of claims 1-17, 20 and 21, under 35 U.S.C. 102(e) as being anticipated by Rosen et al (US2007/015271 filing date 4/2/2003), is withdrawn.

Applicant amendment the claims to recite that the oligonucleotide "consists of" the sequence of SEQ ID NO:1. Rosen discloses a sequence comprising SEQ ID NO:1 and additional sequences. Therefore, Rosen no longer anticipates the claims.

The rejection of claims 11-15, 20 and 21, under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating an inflammatory skin disease comprising administering to a subject in need thereof an effective amount of a CpG oligodeoxynucleotide (ODN) comprising the formula SYYSSAGGTTSNYRAWYTC (SEE ID NO:1), wherein S is G or C; Y is C or T; N is any one selected from the group consisting of A, G, T, and C; R is G or A, W is A or T, and M is A or C, and wherein the CpG ODN comprises at least two unmethylated CpG motifs, does not reasonably provide enablement for a method of treating or preventing any skin disease other than an inflammatory skin disease, is withdrawn.

Applicant amended the claims to recite specifically an inflammatory skin disease, therefore overcoming the enablement issues of record. However, upon further consideration additional issues of enablement need to be addressed. (See below).

Upon further consideration, the following rejection and objections are necessary:

***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-15 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

A) A method of inhibiting a Th2 cytokine and/or inducing a Th1 cytokine, comprising administering to a subject an effective amount of an isolated CpG oligodeoxynucleotide (ODN), wherein said ODN consists of the sequence of SEQ ID NO:1: [formula]  $\text{SYYSSACGTTSNYRAWMYTC}$  (SEQ ID NO:1), wherein S is G or C; Y is C or T; N is any one selected from the group consisting of A, G, T, and C; R is G or A; W is A or T; and M is A or C, and wherein the CpG ODN comprising at least two unmethylated CpG motifs, wherein the ODN is expressed and wherein said administering and expression of the ODN inhibits a Th2 cytokine and/or induces a Th1 cytokine;

B) A method of stimulating an immune response, comprising administering to a subject an effective amount of an isolated CpG oligodeoxynucleotide (ODN), wherein said ODN consists of the sequence of SEQ ID NO:1: [formula]  $\text{SYYSSACGTTSNYRAWMYTC}$  (SEQ ID NO:1), wherein S is G or C; Y is C or T; N is any one selected from the group consisting of A, G, T, and C; R is G or A; W is A or T; and M is A or C, and wherein the CpG ODN comprising at least two unmethylated CpG motifs, wherein the ODN is expressed and wherein said administering and expression of the ODN stimulates an immune response;

C) A method for treating an inflammatory skin disease in a subject, comprising administering to a site of inflammatory skin disease in a subject an effective amount of an isolated CpG oligodeoxynucleotide (ODN), wherein said ODN consists of the sequence of SEQ ID NO:1: [formula]  $\text{SYYSSACGTTSNYRAWMYTC}$  (SEQ ID NO:1), wherein S is G or C; Y is C or T; N is any one selected from the group consisting of A,

G, T, and C; R is G or A; W is A or T; and M is A or C, and wherein the CpG ODN comprising at least two unmethylated CpG motifs, wherein the ODN is expressed and wherein said administering and expression of the ODN are correlated with an improvement of an inflammatory skin disease symptom in said subject, does not reasonably provide enablement for 1) a method of inhibiting a Th2 cytokine and/or inducing a Th1 cytokine or a method of stimulating an immune response that does not have a result; 2) a method that administers an ODN but does not express the ODN; and 3) a method for treating an inflammatory skin disease that administers the CpG ODN to the subject but not the site of inflammatory skin disease. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

While determining whether a specification is enabling, one considers whether the claimed invention provides sufficient guidance to make or use the claimed invention, if not, whether an artisan would require undue experimentation to make and use the claimed invention and whether working examples have been provided. When determining whether a specification meets the enablement requirements, some of the factors that need to be analyzed are: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill, the level of predictability in the art, the amount of direction provided by the inventor, the existence of working examples, and whether the quantity of any necessary experimentation to make or use the invention based on the content of the disclosure is "undue".

1) Claim 1 recites a method of inhibiting a Th2 cytokine and/or inducing a Th2 cytokine. Claim 7 recites a method of stimulating an immune response. Both claims do not recite a result in the active methods steps. Therefore, the breadth of the claims encompasses a method with no result.

However, the specification teaches that the intended use of these methods is to induce an immune response. The specification fails to provide an enabled use for a method of inhibiting a Th2 cytokine and/or inducing a Th1 cytokine and a method of stimulating an immune response that does not have the result of inhibiting a Th2 cytokine and/or inducing a Th1 cytokine or stimulating an immune response as encompassed by the breadth of the claims.

2) The claims recite an active step of administering an ODN without the requirement that the ODN be expressed. Therefore, the breadth of the claims encompasses administering an ODN without expressing the ODN. However, the specification teaches that the ODN must be expressed to stimulate an immune response. Therefore, since the specification teaches that expression of the ODN is required, a method that only administers the ODN but does not express the ODN will not function and thus is not enabled.

3) The claims recite "administering to a subject in need thereof an effective amount of an isolated CpG oligodeoxynucleotide" without the requirement that the ODN be delivered to the site of the inflammatory skin disease. Therefore the breadth of the claims encompass administering the ODN to a secondary site, such as oral administration, to treat a primary site of inflammatory skin disease.

The specification discloses a topical formulation of an ODN that is directly administered to skin lesion in NC/Nga mice, which are a model for atopic dermatitis. The specification discloses that following 5 to 7 days of topical treatment of the lesions, the lesions disappeared, with a significant decrease in hyperkeratosis and acanthosis (p. 33, Example 5, line 21 to p. 34, line 16). Therefore, the specification provides specific guidance to teach a method that directly administers the ODN to the site of an inflammatory skin disease that successfully improves a symptom of inflammatory skin disease in a subject. However, the specification fails to provide specific guidance to teach a means of administering the ODN to a secondary site that is not the site of inflammatory skin disease that successfully improves a symptom of inflammatory skin disease as is encompassed by the claims.

The art teaches that while many advances in delivering therapeutic nucleic acids to subjects, method of administration of nucleic acid to a target site that do not deliver directly to the site of action are unpredictable. Tomasoni and Benigni (Current Gene Therapy 4: 115, col 1 lines 4-7) state, "the success of gene therapy largely depends on an efficient delivery system for the transfer and expression of the therapeutic gene in the target organ or tissue." Many forms of vector delivery to a body site have been described in the art, but very few predictably deliver a therapeutic dose of a vector to the site of treatment. Gautam et al (Am J Respir Med, 1(1) abstract) discloses the use of different vector delivery routes to the lung, such as intravenous injection, intratracheal installation, and aerosol with varying degrees of success. They further disclose various barriers to delivery of vectors such as serum proteins during intravenous injection,

surfactant and mucus interference during more topical applications of vectors. There have also been the problem of immune and cytokine responses against the vector delivery vehicle obstructing delivery of gene therapies. Yang discloses barriers to the use of various catheters in gene delivery during vascular gene therapy stating low transfection efficiency, high prevalence of tissue injury, and poor control of delivery to the cells of targeted vessels (Radiology, 228(1) p. 38 col 1 lines 1 and 2, p 39 col 1 lines 22-31 and lines 50-55, 2003). Because many problems are associated with the modes of delivering a vector to a targeted body site, methods of indirect delivery are generally deemed unpredictable.

In conclusion, the specification fails to provide specification guidance to teach a method that indirectly delivers a therapeutic dose of the ODN to a site of skin inflammation that improves a symptom of inflammatory skin disease and the art teaches that such indirect routes of administration are unpredictable in the art. Therefore, the specification and the art fail to provide enablement for such embodiments. The specification provides specific guidance to a method that administers the ODN to the site of inflammatory skin disease in a subject that provides for improvement of a symptom of inflammatory skin disease. Therefore, the specification only provides enablement for a method for treating a inflammatory skin disease that administers to the site of inflammatory skin disease in a subject and does not enable a method that generally administers the ODN to a subject.

Therefore at the time of filing the skilled artisan would need to perform an undue amount of experimentation without a predictable degree of success to implement the invention as claimed.

Applicant's arguments filed 11/5/2009 have been fully considered but they are not persuasive. Applicant asserts that the amendment to the claims address the issues of enablement. Applicant's argument is not found persuasive because while the amendments address some of the issues of enablement, addition enablement issues remain, as discussed above.

### ***Double Patenting***

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claim 17 is objected to under 37 CFR 1.75 as being a substantial duplicate of claim 16. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is

proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claims 16 and 17 only differ in their recited intended use. The claims composition of claims 16 and 17 are structurally identical and thus are both directed to the same product. Thus, because the claim recites structurally identical products and the intended uses recites by the claims do not impart a distinguishable structural difference between the products of claims 16 and 17, the claims are duplicates of each other.

Cancelling one of the claims, amending the claims to recite a distinguishable structural difference between the products, or adding the limitations of claim 17 to claim 16 would be remedial.

***Allowable Subject Matter***

Claims 1-10 are allowable.

Claims 11-17 are not allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MARCIA S. NOBLE whose telephone number is (571)272-5545. The examiner can normally be reached on M-F 9 to 5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on (571) 272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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